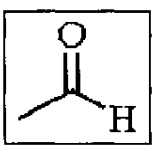
Acetaldehyde



[75-07-0] · C_2H_4O · Acetaldehyde · (MW 44.05)

(reagent used as two-carbon electrophilic component in a wide array

Physical Data: mp -123.5 °C; bp 21 °C; *d* 0.788 g cm^{-3}.

Solubility: sol H_2O, alcohol, ether, and most organic solvents.

Form Supplied in: colorless liquid; widely available.

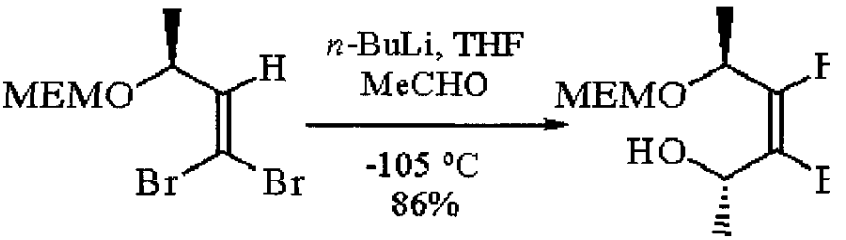
Purification: shaken with powdered $NaHCO_3$ for 30 min; dried over 760 mmHg through a 70 mm Vigreux column.

Handling, Storage, and Precautions: bottles may develop pressure a To help prevent polymerization and autoxidation, store under nitroge Acetaldehyde is a cancer suspect agent and should be used only in a (oral) rat LD_{50}: 661 mg kg^{-1}. Incompatible with strong acids, strong b Decomposes on prolonged exposure to air.

1,2-Additions.

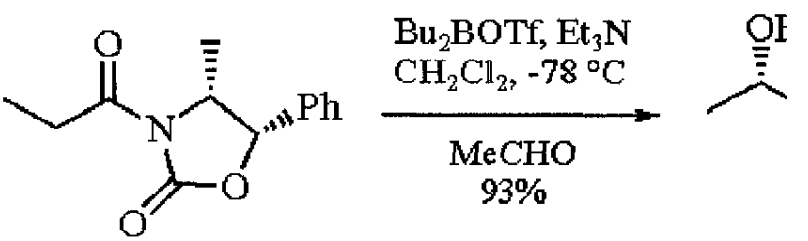
Acetaldehyde reacts with a myriad of nucleophilic reagents, generall two-carbon extended secondary alcohols. Aryl-,[1] alkynyl-,[2] and alky acetaldehyde even at low temperature. A chiral vinyllithium reagent stereoselectively to afford a 10:1 mixture of diastereomeric alcohols reagents behave in an analogous manner with acetaldehyde to give th ketones[7] upon subsequent oxidation. Allyl organometallics react wit

depending on the metal and conditions to give the corresponding hon allylboronates also react with acetaldehyde at -78 °C to afford the ho enantioselectivity.[9] *trans*-Epoxides are produced selectively through acetaldehyde with halomethyl sulfones under basic phase transfer co reagents[11] and Horner-Emmons phosphonate[12] ylides react with ace



Aldol Additions.

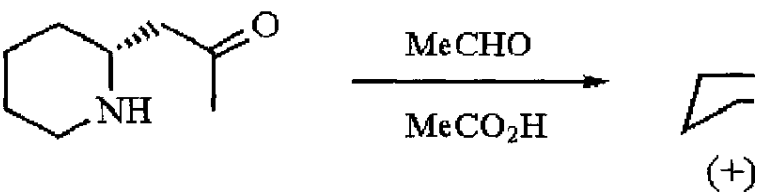
Acetaldehyde serves as an electrophilic partner in the aldol condensa Knoevenagel condensation of acetaldehyde with active methylene co provides good yields of the ethylidene substituted compounds.[14] Ad methylene compound to acetaldehyde results in a Michael addition o initially formed ethylidene.[15] Tollens reaction of acetaldehyde with f pentaerythritol.[16] The addition of acetaldehyde in a Baylis-Hillman c using ***1,4-Diazabicyclo[2.2.2]octane*** (DABCO) as catalyst gives a 9(stereoselective aldol reaction of acetaldehyde with achiral[18] and chir much attention and is a proven method for controlling acyclic relativ For example, the boron enolate of a norephedrine-derived propionyl to afford in 90% yield and >98% de the *syn* aldol product (eq 2).[19a] undergoes nitro-aldol condensation to the corresponding nitro alcoho variety of heterocycles react with acetaldehyde to give good yields o zinc,[22] copper,[23] and boron[24] enolates of esters and ketones provide



Mannich and Mannich-Type Reactions.

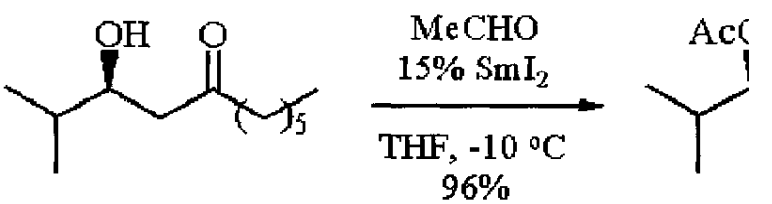
Although not as commonly used as ***Formaldehyde***, acetaldehyde un

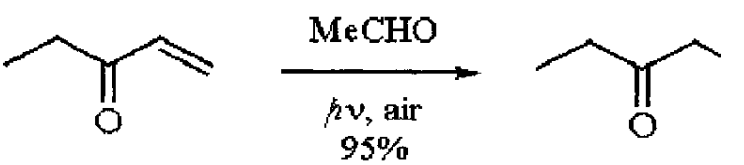
Mannich reactions. Intramolecular Mannich reaction of acetaldehyde natural product myrtine (eq 3).[25] The intramolecular Mannich reactic synthesis of proline derivatives.[26] Nucleophiles as diverse as dialkyl radicals[29] may also add to the intermediate imine of acetaldehyde in historically significant reaction of acetaldehyde in this mode is the St cyanide is added to the adduct of ammonia and acetaldehyde followe α-aminonitrile.[30] The Pictet-Spengler reaction utilizing acetaldehyde reaction. Acetaldehyde has been extensively used in the synthesis of from tryptophan derivatives through this cyclization.[31] Other ring sy tetrahydroisoquinolines[32] and dihydrooxazines[33] have also been forn cyclization with acetaldehyde.



Metal and Other Promoted Condensations.

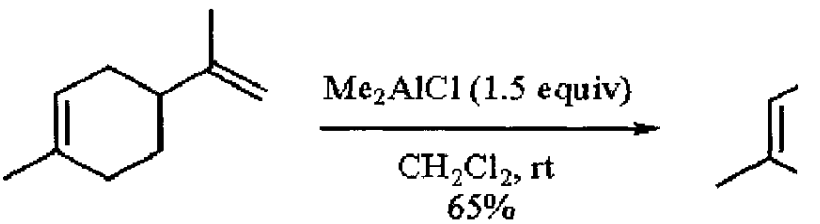
In the mixed Tishchenko reaction using ***Aluminum Isopropoxide*** as predominately the oxidized partner. Thus when condensed with benz major product.[34] Recently an interesting and synthetically useful ster Tishchenko reduction of β-hydroxy ketones using acetaldehyde and affording *anti*-1,3-diol monoacetates, has been reported (eq 4).[35] The coupling of acetaldehyde with other higher-order aldehydes that cont been achieved using a vanadium(II) reagent.[36] The photochemical ac presence of molecular oxygen to α,β-unsaturated esters and ketones dicarbonyl compounds (eq 5).[37]





Pericyclic Reactions.

The thermal ene reactions of acetaldehyde and other aliphatic aldehy very productive.[38] However, acetaldehyde can be induced to undergo alkenes under Lewis acid activation. ***Dimethylaluminum Chloride*** h reaction between the relatively reactive 1,1-di-, tri-, and tetrasubstitu unreactive monosubstituted terminal alkenes, the more Lewis acidic employed to obtain reasonable yields of ene products with acetaldeh unreactive dieneophile towards dienes. The hetero-Diels-Alder reacti reported under high pressure acceleration with 1-alkoxydienes to affo with modest *endo* selectivity.[41]



Paraldehyde and Other Acetaldehyde Deri

Paraldehyde has historically been used as a stabile and less volatile f of chemical reactions.[42] However, since its classification as a control availability has led to its limited use in modern synthetic organic che generated from paraldehyde through acid catalyzed degradation of th distillation.[43] The diethyl acetal of acetaldehyde, commonly known a acetaldehyde or paraldehyde, ethanol, and calcium chloride.[44] Acetal been used for the protection of diols as their ethylidene acetals.[45]

Related Reagents.

Acetaldehyde N-t-Butylimine; ***Acetaldoxime***; ***Crotonaldehyde***; ***Dim Vinyl Ether***; ***Formaldehyde***; ***Formaldehyde-Dimethylamine***; ***Vinyl***

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1. (a) Trécourt, F.; Marsais, F.; Güngör, T.; Quéguiner, G. *JCS(P1)* **1** M.; Parsiot, D. *H* **1990**, *31*, 1485.
2. Marshall, J. A.; Wang, X.-J. *JOC* **1991**, *56*, 960.
3. (a) Walter, L. A. *OSC* **1955**, *3*, 757. (b) Oppolzer, W.; Snowden, R F.; Khanolkar, A. D. *JOC* **1990**, *55*, 6058.
4. Mahler, H.; Braun, M. *CB* **1991**, *124*, 1379.
5. (a) Overberger, C. G.; Saunders, J. H.; Allen, R. E.; Gander, R. *OS* Munno, A.; Pocci, M. *JCS(P1)* **1976**, 570.
6. Drake, N. L.; Cooke, G. B. *OSC* **1943**, *2*, 406.
7. Sugai, T.; Kakeya, H.; Ohta, H. *JOC* **1990**, *55*, 4643.

8. (a) Hoffman, R. W. *AG(E)* **1982**, *21*, 555. (b) Coxon, J. M.; van E
6121. (c) Doxsee, K. M.; Mouser, J. K. M. *TL* **1991**, *32*, 1687.
9. (a) Roush, W. R.; Grover, P. T.; Lin, X. *TL* **1990**, *31*, 7563. (b) Sti
759.
10. Hewkin, C. T.; Jackson, R. F. W. *TL* **1990**, *31*, 1877.
11. Speziale, A. J.; Ratts, K. W. *JACS* **1962**, *84*, 854.
12. (a) Motoyoshiya, J.; Yazaki, T.; Hayashi, S. *JOC* **1991**, *56*, 735. (
A.; Rainford, D.; Smith, A. M. *SL* **1990**, 531.
13. Heathcock, C. H. In *Asymmetric Synthesis*; Morrison, J. D., Ed.;
pp 111-212.
14. Fones, W. S. *OSC* **1963**, *4*, 293.
15. (a) Kent, R. E.; McElvain, S. M. *OSC* **1955**, *3*, 591. (b) Horning,
OSC **1955**, *3*, 317. (c) Oikawa, Y.; Hirasawa, H.; Yonemitsu, O. *TL*
16. Schurink, H. B. J. *OSC* **1932**, *1*, 425.
17. Yadav, J. S.; Ravishankar, R. *TL* **1991**, *32*, 2629.
18. Kishikawa, K.; Sankhavasi, W.; Yamamoto, M.; Kohmoto, S.; Y
19. (a) Evans, D. A.; Dow, R. L.; Shih, T. L.; Takacs, J. M.; Zahler,
Sankhavasi, W.; Yamamoto, M.; Kohmoto, S.; Yamada, K. *BCJ* **199**
TL **1991**, *32*, 2577.
20. (a) Ballini, R. *JCS(P1)* **1991**, 1419. (b) Ono, N.; Kawamura, H.;
1990, *46*, 7483.
21. (a) Amberg, W.; Seebach, D. *CB* **1990**, *123*, 2413. (b) Reissig, H
(c) West, F. G.; Fisher, P. V.; Willoughby, C. A. *JOC* **1990**, *55*, 593
22. Lambert, F.; Kirschleger, B.; Villiéras, J. *JOM* **1991**, *406*, 71.
23. (a) Ito, T.; Okamoto, S.; Sato, F. *TL* **1990**, *31*, 6399. (b) Heng, K.
24. Boldnini, G. P.; Mancini, F.; Tagliavini, E.; Trombini, C.; Umani
25. Slosse, P.; Hootelé, C. *TL* **1978**, 397.
26. Capasso, R.; Randazzo, G.; Pecci, L. *CJC* **1983**, *61*, 2657.
27. Courtois, G.; Miginiac, L. *SC* **1991**, *21*, 201.
28. Katritzky, A. R.; Latif, M.; Urogdi, L. *JCS(P1)* **1990**, 667.
29. Clerici, A.; Porta, O. *TL* **1990**, *31*, 2069.
30. Kendall, E. C.; McKenzie, B. F. *OSC* **1932**, *1*, 21.
31. (a) Shiqi, P.; Min, G.; Winterfeldt, E. *LA* **1993**, 137. (b) Leete, E.
M.; Deng, L.; Cook, J. M. *TL* **1992**, *33*, 4721. (d) Zhang, F.; Goyal,
JMC **1992**, *35*, 82. (e) Behforouz, M.; West, S. J.; Chakrabarty, C.;
1992, *34*, 483. (f) Hermkens, P. H. H.; van Maarseveen, J. H.; Cobbe
Kruse, C. G.; Scheeren, H. W. *T* **1990**, *46*, 833. (g) Bates, H. A.; Bag
51, 3061.
32. (a) Kametani, T.; Ujiie, A.; Ihara, M.; Fukumoto, K. *JCS(P1)* **19**
E.; Badia, M. D.; Villa, M. J.; Castedo, L.; Dominguez, D. *T* **1987**, *4*
33. Sabie, R.; Fillion, H.; Pinatel, H.; Fenet, B. *JHC* **1990**, *27*, 1893.
34. Lin, I.; Day, A. R. *JACS* **1952**, *74*, 5133.
35. Evans, D. A.; Hoveyda, A. H. *JACS* **1990**, *112*, 6447.
36. (a) Konradi, A. W.; Pedersen, S. F. *JOC* **1990**, *55*, 4506. (b) Park
5924.
37. Macias, F. A.; Molinillo, J. M. G.; Collado, I. G.; Massanet, G. M
3063.
38. Mikami, K.; Shimizu, M. *CRV* **1992**, *92*, 1021.
39. (a) Snider, B. B.; Rodini, D. J. *TL* **1980**, *21*, 1815. (b) Cartaya-M
B. B. *JOC* **1984**, *49*, 2443.
40. Snider, B. B.; Phillips, G. B. *JOC* **1983**, *48*, 464.

41. (a) Makin, S. M.; Él'yanov, B. S.; Raifel'd, Y. E. *IZV* **1974**, 2654.
Flipek, S. *S* **1979**, 41. (c) Raifel'd, Y. E.; Él'yanov, B. S.; Makin S. M
42. (a) Emerson, W. S.; Patrick, T. M., Jr. *OSC* **1963**, *4*, 980. (b) Fon
Dolder, M.; Xie, S.; Tamm, C. *HCA* **1990**, *73*, 63. (d) Long, F. A.; H
Ronzio, A. R.; Waugh, T. D. *OSC* **1955**, *3*, 438. (f) Frank, R. L.; Pilg
4, 451. (g) Spivey, A. M.; Curd, F. H. S. *JCS* **1949**, 2656. (h) Wong,
Rytting, J. H.; Higuchi, T. *JPS* **1988**, *77*, 967.
43. Drake, N. L.; Cooke, G. B. *OSC* **1943**, *2*, 407.
44. Adkins, H.; Nissen, B. H. *OSC* **1932**, *1*, 1.
45. Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Syn*
1991; p 120.

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